A Phase 3, Multicenter, Open-Label, Randomized Study of Nemvaleukin Alfa in Combination With Pembrolizumab Versus Investigator's Choice Chemotherapy in Patients With Platinum-Resistant Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer (ARTISTRY-7)

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Evaluate the antitumor activity of nemvaleukin alfa (*nemvaleukin*, ALKS 4230) in combination with pembrolizumab as compared with chemotherapy in patients with platinum-resistant ovarian cancerSecondary Objectives:Evaluate the antitumor activity of...

Ethical review	Not approved
Status	Will not start
Health condition type	Reproductive neoplasms female malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON51689

Source
ToetsingOnline

Brief title
ARTISTRY-7

Condition

- Reproductive neoplasms female malignant and unspecified

Synonym
Fallopian tube cancer, Ovarian cancer, Peritoneal cancer

Research involving
Human

Sponsors and support

Primary sponsor: Alkermes Inc.
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Epithelial Ovarian Cancer, Nemvaleukin Alfa, Pembrolizumab, Peritoneal Cancer

Outcome measures

Primary outcome

Primary Endpoint:

• Progression-free survival (PFS) as assessed by Investigator, based on

Response Evaluation Criteria in Solid Tumors (RECIST) v1.1

Secondary outcome

Key Secondary Endpoints:

• Objective response rate (ORR) as assessed by Investigator, based on RECIST

v1.1

Other Secondary Endpoints:

• Overall Survival (OS)

• Disease control rate (DCR), duration of response (DOR), and time to response

(TTR) as assessed by Investigator, based on RECIST v1.1

• Cancer antigen (CA)-125 response as defined by the Gynecologic Cancer

InterGroup (GCIG)

• Safety as assessed by treatment-emergent adverse events (TEAEs), clinical

laboratory parameters, vital signs, and electrocardiograms (ECGs)

Study description

Background summary

This is a Phase 3, multicenter, open-label, randomized study of nemvaleukin in combination with pembrolizumab versus protocol-specific Investigator*s choice chemotherapy in patients with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer.
All subjects will attend a Screening Visit, at which informed consent will be obtained, eligibility will be assessed, and demographics, medical history, prior and concomitant medications, and prior procedures will be reviewed and recorded. If tumor tissue is to be collected for central testing of PD-L1 status prior to Screening, a pre-screening informed consent form will be obtained. For the purposes of confirming the diagnosis of epithelial ovarian cancer (EOC) and for evaluating pretreatment tumor expression of genes and/or proteins of interest (eg, PD-L1 status, TMB, and microsatellite instability [MSI]), an initial tumor biopsy will be obtained prior to the start of treatment, if such tissue is not already available. Archival tissue can be used in place of pretreatment biopsy. PD-L1 status via central vendor will be required prior to randomization.

Study objective

Evaluate the antitumor activity of nemvaleukin alfa (*nemvaleukin*, ALKS 4230) in combination with pembrolizumab as compared with chemotherapy in patients with platinum-resistant ovarian cancer

Secondary Objectives:
Evaluate the antitumor activity of nemvaleukin in combination with pembrolizumab as compared with chemotherapy
Evaluate the safety of nemvaleukin in combination with pembrolizumab as compared with chemotherapy

Study design

Subjects will be centrally allocated in a randomized fashion (3:1:1:3) to receive either:
• Arm 1: nemvaleukin and pembrolizumab combination therapy
• Arm 2: pembrolizumab monotherapy
• Arm 3: nemvaleukin monotherapy
• Arm 4: Investigator*s choice chemotherapy. Options for protocol-specific Investigator*s choice chemotherapy include one of the following: pegylated

liposomal doxorubicin (PLD), paclitaxel, topotecan, or gemcitabine. The Investigator will pre-select the Investigator*s choice treatment before the randomization of each patient.
To ensure equal distribution of prognostic factors in the study arms, patients will be stratified according to the following parameters:
• PD-L1 status (immunohistochemistry CPS >=10 vs CPS <10)
• Histological subtype (high-grade serous vs non-high-grade serous)
• Investigator*s choice chemotherapy (paclitaxel vs other chemotherapies)

Intervention

Subjects will be centrally allocated in a randomized fashion (3:1:1:3) to receive either:
• Arm 1: nemvaleukin and pembrolizumab combination therapy
• Arm 2: pembrolizumab monotherapy
• Arm 3: nemvaleukin monotherapy
• Arm 4: Investigator*s choice chemotherapy. Options for protocol-specific Investigator*s choice chemotherapy include one of the following: pegylated liposomal doxorubicin (PLD), paclitaxel, topotecan, or gemcitabine. The Investigator will pre-select the Investigator*s choice treatment before the randomization of each patient.

Study burden and risks

Please refer to the table of procedures on p. 16 of the protocol (v2.0_05Oct2021).

This study will take 2 years with a follow-up for 3 years. Depending on the treatment the subject will receive, he/she will have to visit the hospital 51 - 183 times. During these visits there will be extra procedures and tests which means that the hospital visits will take longer than usual. A visit will take 1-4 hours.

Additionally, participation in this study may affect the subject's eligibility for enrolling in a subsequent clinical trial.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Patient is female and >=18 years of age.
2. Patient or patient's legal representative is willing and able to provide written informed consent.
3. Patient is willing and able to comply with scheduled visits, treatment schedule, laboratory tests, and other requirements of the study.
4. Patient has histologically confirmed diagnosis of EOC (i.e., high-grade serous, endometrioid of any grade, clear cell), fallopian tube cancer, or primary peritoneal cancer.
5. Patient has platinum-resistant/refractory disease, defined as disease progression within 180 days following the last administered dose of platinum therapy beyond first-line setting (resistant) or lack of response or disease progression while receiving the most recent platinum-based therapy (refractory). Patient must have progressed radiographically on or after their most recent line of anticancer therapy.
a. Note: Progression should be calculated from the date of the last administered dose of platinum therapy to the date of the radiographic imaging showing progression.
b. Note: Patients who have platinum-refractory or platinum-resistant disease to frontline treatment are excluded.
6. Patient must have received at least 1 prior line of systemic anticancer therapy in the platinum sensitive setting, and no more than 5 prior lines of

systemic anticancer therapy in the platinum-resistant setting. Patient must have received at least 1 line of therapy containing bevacizumab.
The following guidelines apply:
a. Prior PARP inhibitor is allowed if included within these limits of prior therapy. Prior PARP inhibitor is required for patients with a breast cancer gene (BRCA) mutation.
b. Adjuvant ± neoadjuvant is considered 1 line of therapy.
c. Maintenance therapy (eg, bevacizumab, PARP inhibitors) will be considered part of the preceding line of therapy (i.e., not counted independently).
d. Therapy that changed due to toxicity in the absence of progression will be considered part of the same line (ie, not counted independently).
e. Hormonal therapy will be counted as a separate line of therapy unless it was given as maintenance therapy.
f. Patients having received only 1 line of platinum-based therapy must have received at least 4 cycles of platinum, must have had a response (complete response [CR] or partial response [PR]) and then progressed >3 to <=6 months after the date of the last dose of platinum.
7. Patient has at least one measurable lesion that qualifies as a target lesion based on RECIST v1.1. Tumor lesions situated in a previously irradiated area, or in an area subjected to other loco-regional therapy, are not considered measurable unless there has been demonstrated progression in the lesion.
8. Patient is willing to undergo a pre-treatment tumor biopsy or provide qualifying archival tumor tissue. All pretreatment tissue must have been collected no more than 120 days prior to screening. Central testing of PD-L1 status will be required prior to randomization.
9. Patient has recovered from the effects of any previous chemotherapy, immunotherapy, other prior systemic anticancer therapy, radiotherapy, and/or surgery (i.e., residual toxicity no worse than Grade 1 [Grade 2 treatment-associated peripheral neuropathy and/or any grade of alopecia are acceptable assuming all other inclusion criteria are met]).
10. Patient who has received prior systemic anti-neoplastic agent(s) must wait at least 5 half-lives or 4 weeks (whichever is shorter) following prior therapy before enrollment into the study or 4 weeks if the half-life of a given investigational agent is not known.
11. Patient has an Eastern Cooperative Oncology Group (ECOG) status of 0 or 1 and an estimated life expectancy of at least 3 months.
12. Patient has adequate hematologic reserve as described in the protocol.
13. Patient has adequate hepatic function, as evidenced by aspartate transaminase (AST) and alanine transaminase (ALT) values <=3 × the upper limit of normal (ULN) and serum total bilirubin values of <=1.5 × ULN (<=2 × ULN for patients with known Gilbert's syndrome). For patients with documented baseline liver metastasis, the following limits will apply: <=5 × ULN for transaminase and <=2 × ULN for bilirubin.
14. Patient has adequate renal function, as evidenced by a serum creatinine <=1.5 × ULN or a calculated creatinine clearance of >=45 mL/min by the Cockcroft-Gault Equation.
15. Patient has international normalized ratio (INR) and/or prothrombin time

and activated partial thromboplastin time (aPTT) <=1.5 × ULN unless the patient is receiving anticoagulant therapy, in which case INR and/or prothrombin time and aPTT must be within the desired therapeutic range of intended use for such anticoagulants.
16. Patient agrees to abide by the contraceptive requirements detailed in the protocol.
17. Women of childbearing potential (WOCBP) must have a negative pregnancy test (serum or urine). (See Appendix 1 in Protocol for the definition of WOCBP.)

Exclusion criteria

1. Patient has primary platinum-refractory disease or primary platinum resistance, defined as disease progression during first-line platinumbased therapy (refractory) or disease progression <3 months after completion of first-line platinum-based therapy (resistant).
2. Patient has histologically confirmed diagnosis of EOC with mucinous or carcinosarcoma subtype.
3. Patient has nonepithelial tumor (eg, germline or stromal cell tumor) or ovarian tumor with low malignant potential (i.e., borderline or lowgrade serous tumor).
4. Patient requires fluid drainage (eg, paracentesis, thoracentesis, pericardiocentesis) of >=500 ml within 6 weeks of first dose of study drug.
5. Patient has received prior IL-2-based or IL-15-based cytokine therapy; patient has had exposure, including intralesional, to IL-12 or analogs thereof.
6. Patient has prior exposure to any antiPD1/PDL1 therapy.
7. Patient requires or has taken systemic corticosteroids (>10 mg of prednisone daily, or equivalent)within 14 days prior to the first dose of study drug(s); however, replacement doses, topical, ophthalmologic, and inhalational steroids are permitted.
8. Patient has taken non-steroid systemic immunomodulatory agents (eg, etanercept, adalimumab, etc.) within 28 days prior to the first dose of study drug(s), or anticipates any use of these therapies during the study period.
9. Patient has undergone any major surgical procedure within 3 weeks prior to Screening. Patients who have not recovered from any previous surgery that occurred more than 3 weeks prior to Screening are also excluded.
10. Patient has undergone prior solid organ and/or non-autologous hematopoietic stem cell or bone marrow transplant.
11. Patient has received a live or live-attenuated vaccine(s) within 30 days prior to the first dose of study drug(s). Note: Coronavirus Disease 2019 (COVID-19) vaccine is allowed; see guidance on COVID-19 vaccines in Section 7.3.2).
12. Patient has had any active infection and/or a fever >=38.5°C (>=101°F) within 3 days prior to the first dose of study drug(s) requiring systemic therapy. Antibiotics given for periprocedural prophylaxis or given presumptively for a limited time (eg, until infection was ruled out), as well as topical or

intra-ocular antibiotics, shall not be
exclusionary.
13. Patient has active autoimmune disease(s) requiring systemic treatment within the past 2 years or a documented history of clinically severe autoimmune disease that has required chronic or frequent systemic steroids. Replacement therapy (eg, thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency) is allowed.
14. Patient has underlying chronic lung disease, chronic obstructive pulmonary disease, metastatic lung disease, pleural effusions, or other lung disorders (eg, pulmonary embolism) with a baseline room air oxygen saturation of <92% at screening and/or dyspnea (>=Grade 3) which requires oxygen therapy.
15. Has a history of (noninfectious) pneumonitis that required steroids or has current pneumonitis.
16. Patient has any other concurrent uncontrolled illness or laboratory findings that may interfere with the planned treatment, affect patient compliance, such as recent serious trauma, or mental illness or substance use, which may interfere with the ability of the patient to cooperate and participate in the study.
17. Patient is at high risk of treatment-related complications as described in the protocol.
18. Patient has had an active second malignancy within the previous 2 years.
19. Patient is currently breastfeeding or is planning to become pregnant or to begin breastfeeding during the study period or within 120 days after last study drug administration.
20. Patient has active or symptomatic central nervous system (CNS) metastases as described in the protocol.
21. Patient has known or suspected hypersensitivity to pembrolizumab or to any component(s) of pembrolizumab or nemvaleukin.
22. Patient has active uncontrolled coagulopathy.
23. Patient has QT interval corrected by the Fridericia Correction Formula values of >470 msec; patient who is known to have congenital prolonged QT syndromes; or patient who is on medications known to cause prolonged QT interval on ECG.
24. Patient is known to be positive for human immunodeficiency virus.
25. Patients with known active hepatitis B (eg, hepatitis B surface antigen [HBsAg] reactive) are excluded.
26. History of bowel obstruction (including sub-occlusive disease) related to the underlying ovarian disease, history of abdominal fistula, gastrointestinal perforation or intra-abdominal abscess, or evidence of recto-sigmoid involvement or bowel involvement on computed tomography (CT) scan.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	13
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Nemvaleukin Alfa
Generic name:	Nemvaleukin Alfa
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Paclitaxel
Generic name:	Taxol, Abraxane
Product type:	Medicine
Brand name:	Pegylated Liposomal Doxorubicin (PLD)
Generic name:	driamycin®, Rubex®
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Pembrolizumab
Generic name:	Keytruda®
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Topotecan
Generic name:	Hycamtin

Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	16-06-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Not approved Date:	06-12-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2021-002326-24-NL
ClinicalTrials.gov	NCT05092360
CCMO	NL80784.056.22